TABLE I (*Continued*)

INDANYL SULFIDES, SULFOXIDES, AND SULFONES
'Indanyl-SO_x—R'

No.	Found C	Found H	Found S	Infrared Absorption Peaks (Microns)								
I	80.11	6.25	13.9	5.27	5.44	6.3	5.58			9.2	9.38	9.78
II[c]	79.18	6.24	14.0	5.22	5.33	6.3	5.53			9.2	9.38	9.78
III	80.72	6.67	13.3	5.27	5.46	6.25	5.60			9.18		9.84
IV[d]	79.56	7.02	13.4	5.25	5.55	6.25				9.18		9.84
V[e]	68.79	5.17	11.9	5.26	5.43	6.35				9.15		9.9
VI	83.23	5.89	11.2	5.24	5.43	6.15, 6.3	5.57			9.15		9.8
VII[f]	75.47	8.97	15.4	5.24	5.42	6.21, 6.27	5.57			9.13		9.76
VIII	74.89	6.34	12.8			6.25	7.68	7.87		9.25	9.75	9.9
IX[g]	64.64	4.83	11.4			6.3	7.6	7.85		9.2	9.7	9.9
X	69.01	5.83	11.8			6.3	7.65	7.8	8.75	9.23		9.8
XI	68.94	5.53	12.9			6.21, 6.28	7.65	7.75	8.85	9.25	9.79	10.01
XII	70.41	5.91	11.3			6.25	7.7		8.8	9.25		9.9
XIII	70.01	5.95	11.4									
XIV[h]	61.73	4.75	10.9			6.3	7.6	7.85	8.75	9.25		9.9
XV	74.08	5.51	9.7			6.15, 6.3	7.65	7.8	8.75	9.35		
XVI	65.73	7.69	12.8			6.21, 6.3	7.60	7.78	8.85	8.95		

anhydride and 10 ml. of acetic acid. Aqueous 30% hydrogen peroxide (11.4 g., 0.01 mole) was added to the sulfide solution at 5°. Then the reaction mixture was kept at that temperature for 24 hr., and at room temperature for an additional 48 hr. After the completion of the reaction, the crystalline 1-indanyl aryl sulfone was precipitated by careful addition of crushed ice. The crude crystalline product was filtered and twice recrystallized from 90% aqueous ethanol. The yields obtained and some of the physical and analytical data of the products obtained are shown in Table I.

When 1-indanyl aryl sulfides were oxidized with the same reagents on a water bath, a smaller yield of the sulfones was realized due to some decomposition.

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Carcinogenic Amine Derivatives Containing Nitrogen-15[1,2]

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Several carcinogens have been found to bind to the protein of tissues in which they cause cancer. Since some chemically related noncarcinogens have also been found to bind to protein, this interaction may well be a necessary but not sufficient requirement for the production of tumors.[3]

In order to study this further, the synthesis of three carcinogens labeled with nitrogen-15 was undertaken. These were 4-acetylaminobiphenyl-N^{15}, 4'-fluoro-4-acetylaminobiphenyl-N^{15}, and *N*-(7-hydroxy-2-fluorenyl)acetamide-N^{15}, a weakly carcinogenic metabolite of the strong carcinogen, *N*-2-fluorenylacetamide.

2-Nitrofluorene-N^{15} had been prepared previously in this laboratory[4] by nitrating fluorene with aqueous nitric acid-N^{15} using acetic anhydride to remove the excess water. No reaction occurred when this method was used with biphenyl. When the reaction was carried out in sulfuric acid solvent or when potassium nitrate-N^{15} and sulfuric acid were used as the source of nitric acid, the material either failed to react or was sulfonated. The only effective nitrating agent proved to be 100% nitric acid-N^{15}. The procedure used for nitrating the biphenyl derivatives was based on the method of Maki and Obayashi.[5] The desired *para* isomers were separated from the *ortho* isomers and unchanged hydrocarbon by trituration with hexane, in which the *para* isomers are not soluble. 2-Acetoxyfluorene was nitrated by a modification of the procedure described by Bryant and Sawicki.[6] The nitro compounds were reduced and acetylated by the usual methods as described in the Experimental section.

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(2) Presented before the Meeting-in-Miniature, Florida Section, American Chemical Society, St. Petersburg, Fla., May 8–9, 1959.

(3) For detailed discussion see E. K. Weisburger and J. H. Weisburger, *Advances in Cancer Research*, Vol. 5, J. P. Greenstein and A. Haddow, editors, Academic Press, Inc., New York, 1958, p. 382.

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Biological testing of these compounds will be carried out by Drs. H. P. Morris and Helen Dyer at the National Cancer Institute. The results will be published elsewhere.

EXPERIMENTAL

Preparation of 100% nitric acid. (a) Isotopic nitric acid,[7] (6.79 g.; 0.108 mole as 52.72 g. of a 12.88% solution containing 62.8 atom % nitrogen-15) was carefully neutralized, with cooling, by addition of 4.32 g. (0.108 mole) of sodium hydroxide dissolved in the minimum amount of water. The water was removed by distillation and the dry salt was treated with concentrated sulfuric acid (18 ml., 0.32 mole). Distillation at atmospheric pressure gave 5.6 g. (0.089 mole) of 100% nitric acid-N^{15} b.p. 80–83° (82% recovery).

(b) Potassium nitrate (14.2 g.; 0.07 mole) containing 97.0 atom % nitrogen-15[7] and 31.1 ml. (0.56 mole) of concentrated sulfuric acid gave, upon distillation, 7.1 g. of 100% nitric acid-N^{15} b.p. 78–82° (81% recovery).

4'-Fluoro-4-nitrobiphenyl-N^{15}. A solution of 100% nitric acid-N^{15} (5.6 g.; 0.09 mole containing 62.8 atom % nitrogen-15) in 5.6 g. of glacial acetic acid was added dropwise with stirring to molten 4-fluorobiphenyl (18.4 g.; 0.107 mole, 20% excess), keeping the temperature between 75–82°. Acetic anhydride (12 ml., 0.13 mole) was then added slowly to remove water of reaction. The mixture was kept at 80° for 4 hr., then poured into ice water. After standing overnight the solid was removed by filtration, washed several times with water and then three times with 100-ml. portions of hexane. Crude yield of 4'-fluoro-4-nitrobiphenyl-N^{15} was 9.8 g. (50% based on the nitric acid used). Recrystallization from 175 ml. of ethanol gave 5.5 g. (28%) m.p. 125–126° (lit.,[8] m.p. 123°).

4'-Fluoro-4-acetylaminobiphenyl-N^{15}. 4'-Fluoro-4-nitrobiphenyl-N^{15} (5.5 g.; 0.025 mole) in 150 ml. of warm ethanol was hydrogenated at low pressure using 0.05 g. Adams' platinum oxide catalyst. The yellow solution was filtered free of catalyst into 20 ml. of concentrated hydrochloric acid. The ethanol was removed by distillation, the residue was taken up in hot water containing a little hydrochloric acid, and the solution filtered through a thin mat of charcoal. Potassium acetate was added to the solution just to turbidity, then acetic anhydride (25 ml.) was added, followed by potassium acetate to *p*H 5–6. Stirring was continued for 2 hr. and after standing overnight the 4'-fluoro-4-acetylaminobiphenyl-N^{15} which had precipitated amounted to 2.65 g. (46.5%) m.p. 206° (lit.[9], m.p. 205–206°).

4-Nitrobiphenyl-N^{15}. To molten biphenyl (15.9 g.; 0.103 mole) at 75° was added dropwise with stirring a solution of 5.4 g. (0.086 mole) of 100% nitric acid containing 97.0 atom % nitrogen-15 in 5.4 g. of glacial acetic acid, keeping the temperature below 80°. When the addition had been completed acetic anhydride (12 ml., 0.13 mole) was slowly added to remove water of reaction, then the mixture was kept at 75–80° for 4 hr. After pouring into ice water and leaving overnight, the water was decanted from the semisolid yellow residue, the residue was triturated three times with 50-ml. portions of hexane to remove unchanged biphenyl and 2-nitrobiphenyl and recrystallized from ethanol, giving 6.0 g. of 4-nitrobiphenyl-N^{15} (35.3% based on the nitric acid consumed), m.p. 113–114° (lit.,[10] m.p. 114°).

4-Aminobiphenyl-N^{15}. A mixture of 4-nitrobiphenyl-N^{15} (6.0 g., 0.03 mole), 175 ml. of ethanol, 2.1 g. of calcium chloride dissolved in 41 ml. of water, 63.6 g. of zinc dust, and 2.0 g. of Norit were refluxed for 3 hr., 1.0 ml. of 85% hydrazine hydrate was added and the mixture filtered to remove the zinc, the residue being washed twice with 25-ml. portions of hot ethanol. The alcoholic filtrates were poured into 2 l. of water and allowed to stand overnight. The white precipitate of 4-aminobiphenyl-N^{15} was filtered off and washed well with water, then air-dried. Yield was 4.6 g. (90%) m.p. 53–54° (lit.,[11] m.p. 50–52°).

4-Acetylaminobiphenyl-N^{15}. 4-Aminobiphenyl-N^{15} (4.6 g.; 0.027 mole) was dissolved with heating in 60 ml. of benzene, decanted from a little insoluble material and treated with 5 ml. of acetic anhydride. A precipitate began to form immediately. After refluxing for 15 min. the clear solution was allowed to cool slowly to room temperature. The white crystals which formed were filtered and washed several times with water, giving 5.2 g. (91%) of 4-acetylaminobiphenyl-N^{15} m.p. 171° (lit.[12], m.p. 171–172°) and containing 97.0 atom % nitrogen-15.

2-Nitro-7-acetoxyfluorene-N^{15}. The literature procedure[6] was modified as follows: A mixture of 5.6 g. (0.025 mole) of 2-acetoxyfluorene and 22.5 g. (0.375 mole) of glacial acetic acid was heated to 80° to effect solution, then allowed to cool to 50°. A solution prepared by adding 1.6 g. (0.025 mole) of 100% nitric acid containing 97.0 atom % nitrogen-15 to 12.8 g. (0.125 mole) acetic anhydride in an ice bath (exothermic reaction) was then added to the 2-acetoxyfluorene solution and an exothermic reaction set in. When the temperature reached 75° the mixture was cooled in an ice bath. After the initial exothermic reaction had subsided the mixture was kept at 70–75° for 5 min., then allowed to stand overnight. The yellow solid was filtered, washed with water until the filtrate was no longer acidic and dried, giving 5.4 g. (80.6%) of 2-nitro-7-acetoxyfluorene-N^{15} m.p. 192–193° (lit.[6], 191–192°).

N-(7-Hydroxy-2-fluorenyl)acetamide-N^{15}. To a boiling solution of 2-nitro-7-acetoxyfluorene-N^{15} (5.4 g.; 0.02 mole) in 1 l. of ethanol was added slowly over a period of 1 hr. a solution of 41.7 g. (0.22 mole) of stannous chloride dissolved in 350 ml. of concentrated hydrochloric acid. The solution was concentrated to one-third its volume, then brought up to one-half its original volume with concentrated hydrochloric acid and allowed to stand overnight. The precipitate was filtered and dissolved in 200 ml. of hot water containing a few drops of stannous chloride–hydrochloric acid solution. The solution was filtered through a mat of charcoal and then brought to *p*H 5–6 with potassium acetate. After addition of 40 ml. of acetic anhydride the mixture was allowed to stand overnight. The precipitate of *N*-(7-hydroxy-2-fluorenyl)acetamide-N^{15} containing 97.0 atom % nitrogen-15 amounted to 2.8 g. (48%) m.p. 229–231° (lit.,[13] m.p. 230–232°).

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A Preparation of 10-Hydroxydecanoic Acid

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The synthesis of 10-hydroxydecanoic acid has been accomplished by three methods.[2–4] The one